CLAIMS

What is claimed is:

1. A method for selectively delivering an agent to arterial smooth muscle cells in a mammal, comprising administering to the mammal a composition comprising
   (a) the agent; and
   (b) a substance which selectively binds an arterial smooth muscle cell-specific surface molecule, wherein said arterial smooth muscle cell-specific surface molecule is selected from the group consisting of an Ephrin family ligand and a Eph family receptor, under conditions appropriate for said substance to selectively bind said arterial smooth muscle cell-specific surface molecule.

2. The method of Claim 1 wherein said arterial smooth muscle cell-specific surface molecule is an Ephrin family ligand.

3. The method of Claim 2 wherein said Ephrin family ligand is EphrinB2.

4. The method of Claim 3 wherein said substance is an antibody or antigen binding fragment thereof which binds to EphrinB2.

5. The method of Claim 1 wherein said agent is an angiogenic agent.

6. The method of Claim 1 wherein said agent is an anti-angiogenic agent.

7. The method of Claim 1 wherein said agent inhibits conditions selected from the group consisting of thrombosis, stenosis, restenosis and formation of atherosclerotic plaques.

8. The method of Claim 1 wherein said agent is selected from the group consisting of a cyclin G1 mutant polypeptide, a p27-p16 chimeric polypeptide, a hepatocyte growth factor, a herpes simplex virus thymidine kinase polypeptide, a cytosine deaminase-5-flurocytosine polypeptide, a non-phosphorylatable retinoblastoma polypeptide, a chimeric pRb2/p130 polypeptide, a p21 polypeptide, a p27 polypeptide, a p53 polypeptide, a dominant negative H-ras polypeptide, an eNOS polypeptide, an iNOS polypeptide, a synthetic double-stranded nucleic acid with high binding affinity for E2F, an anti-sense oligonucleotide to p65, an anti-sense oligonucleotide to basic fibroblast growth factor, an active site inactivated factor VIIa polypeptide, a recombinant tissue factor pathway inhibitor, rapamycin, an antioxidant, a glycoprotein IIb/IIIa receptor antagonist, a calcium channel blocker and a nitric oxide donor.

9. The method of Claim 1 wherein said agent is conjugated to said substance.

10. A transgenic animal wherein the genome of said animal comprises a recombinant nucleic acid encoding an indicator gene, wherein said indicator gene is expressed in arterial smooth muscle cells but is not detectably expressed in venous smooth muscle cells.

11. The transgenic animal of Claim 10 wherein said transgenic animal is a mammal.

12. The transgenic animal of Claim 11 wherein said mammal is selected from the group consisting of a mouse, rat, guinea pig, pig, rabbit and sheep.

13. The transgenic animal of Claim 10 wherein said indicator gene is an Ephrin family ligand gene.

14. The transgenic animal of Claim 13 wherein said Ephrin family ligand is EphrinB2.

15. A method for identifying arterial smooth muscle cells in a transgenic animal, wherein the genome of said animal comprises a recombinant nucleic acid encoding an indicator gene inserted in one or more alleles of *EphrinB2*, comprising

a) detecting expression of the indicator gene; and

b) detecting expression of a smooth muscle cell-specific protein;

wherein those cells that express both the indicator gene and the smooth muscle cell-specific protein are arterial smooth muscle cells.

16. The method of Claim 15 wherein said detecting expression of the indicator gene comprises staining a tissue sample from said transgenic animal with a substance appropriate for detection of expression of the indicator gene.

17. The method of Claim 15 wherein said wherein said smooth muscle cell-specific protein is smooth muscle actin.

18. The method of Claim 17 wherein said smooth muscle actin is detected using an antibody or antigen binding fragment thereof.

19. The method of Claim 15 wherein said transgenic animal is a mammal.

20. The method of Claim 19 wherein said mammal is selected from the group consisting of a mouse, rat, guinea pig, pig, rabbit and sheep.

21. A method of assessing an effect of an agent on arterial smooth muscle cells comprising

a) administering said agent to a transgenic animal, wherein the genome of said animal comprises a recombinant nucleic acid encoding an indicator gene inserted in one or more alleles of *EphrinB2*;

b) observing the effect of the agent by detecting expression of the indicator gene; and

c) comparing it to a suitable control.

22. The method of Claim 21 wherein said agent modulates proliferation of arterial smooth muscle cells.

23. The method of Claim 22 wherein said agent inhibits proliferation of arterial smooth muscle cells.

24. The method of Claim 21 wherein said transgenic animal is a mammal.

25. The method of Claim 24 wherein said mammal is selected from the group consisting of a mouse, rat, guinea pig, pig, rabbit and sheep.

26. A method for identifying an arterial smooth muscle cell in a tissue sample from a mammal, comprising

a) contacting the tissue sample with a first composition which binds to EphrinB2;

b) contacting the tissue sample with a second composition that binds to a protein which is expressed on smooth muscle cells; and

c) detecting expression of said first and second compositions, wherein if said first and second compositions are co-expressed on a cell, the cell is an arterial smooth muscle cell.

27. The method of Claim 26 wherein said first composition is selected from the group consisting of an antibody and an antigen-binding fragment thereof.

28. The method of Claim 26 wherein said second composition is selected from the group consisting of an antibody and an antigen-binding fragment thereof.

29. The method of Claim 28 wherein said second composition is an antibody or antigen-binding fragment thereof which binds smooth muscle actin.

30. The method of Claim 26 further comprising a label conjugated to said first composition, wherein said label is selected from the group consisting of a fluorescent label, a colorimetric label, an enzyme label, an affinity label, an epitope label, a spin label and a chemiluminescent group.

31. The method of Claim 26 further comprising a label conjugated to said second composition, wherein said label is selected from the group consisting of a fluorescent label, a colorimetric label, an enzyme label, an affinity label, an epitope label, a spin label and a chemiluminescent group.

32. A method for isolating arterial smooth muscle cells, comprising

a) dissociating cells of a tissue sample comprising arterial smooth muscle cells;

b) contacting the dissociated cells with a first substance which binds to a cell-surface protein expressed on arterial smooth muscle cells, wherein said cell-surface protein is selected from the group consisting of an Ephrin family ligand and an Eph family receptor;

c) contacting the dissociated cells with a second substance which binds to a cell-surface protein expressed on smooth muscle cells; and

d) separating those cells which have bound both said first and said second substances from those cells which have not bound both said first and second substances, wherein those cells that bind both said first and second substances are arterial smooth muscle cells.

33. The method of Claim 32 wherein said cell-surface protein expressed on arterial smooth muscle cells is an Ephrin family ligand.

34. The method of Claim 33 wherein said Ephrin family ligand is EphrinB2.

35. The method of Claim 32 wherein said first substance is selected from the group consisting of an antibody and an antigen-binding fragment thereof.

36. The method of Claim 32 wherein said second substance is selected from the group consisting of an antibody and an antigen-binding fragment thereof.

37. The method of Claim 36 wherein said second substance is an antibody or antigen-binding fragment thereof which binds smooth muscle actin.

38. Arterial smooth muscle cells isolated using the method of Claim 32.

39. A method for assessing an effect of an agent on arterial smooth muscle cells isolated using the method of Claim 32, comprising

a) adding said agent to said isolated arterial smooth muscle cells; and

b) comparing the effect of said agent on said isolated arterial smooth muscle cells with a suitable control, wherein said suitable control comprises arterial smooth muscle cells in the absence of said agent.

40. A cell line derived from arterial smooth muscle cells which are isolated using the method of Claim 32.

41. A cDNA library produced from isolated arterial smooth muscle cells isolated using the method of Claim 32.

42. An oligonucleotide encoding a targeting molecule, comprising

a) a first nucleic acid sequence comprising a promoter region of EphrinB2; and

b) a second nucleic acid sequence encoding a polypeptide,

wherein said first nucleic acid sequence is operably linked to said second nucleic acid sequence.

43. The oligonucleotide of Claim 42 wherein said polypeptide is selected from the group consisting of a protein and a functional fragment thereof.

44. The oligonucleotide of Claim 42, wherein said second nucleic acid sequence encodes a polypeptide selected from the group consisting of a herpes simplex virus thymidine kinase polypeptide, a non-phosphorylatable retinoblastoma polypeptide, a cyclin-dependent kinase inhibitor polypeptide, a mutant cyclin G1 polypeptide, a nitric oxide synthase polypeptide, a growth arrest homeobox, vascular cyclo-oxygenase polypeptide, a thrombomodulin polypeptide, a

vascular endothelial growth factor, a chimeric p27-p16 polypeptide, a hepatocyte growth factor, a cytosine deaminase-5-flurocytosine polypeptide, a chimeric pRb2/p130 polypeptide, a p21 polypeptide, a p27 polypeptide, a p53 polypeptide, a dominant negative H-ras polypeptide, an eNOS polypeptide, an iNOS polypeptide, an active site inactivated factor VIIa polypeptide and a tissue factor pathway inhibitor polypeptide.

45. A method of inducing expressing of a polypeptide in arterial smooth muscle cells of a mammal, comprising administering to said mammal a targeting molecule, wherein said targeting molecule comprises a first nucleic acid sequence comprising a promoter region of EphrinB2 operably linked to a second nucleic acid sequence encoding said polypeptide.

46. The method of Claim 45 wherein said second nucleic acid sequence encodes a polypeptide selected from the group consisting of a herpes simplex virus thymidine kinase polypeptide, a non-phosphorylatable retinoblastoma polypeptide, a cyclin-dependent kinase inhibitor polypeptide, a mutant cyclin G1 polypeptide, a nitric oxide synthase polypeptide, a growth arrest homeobox, vascular cyclo-oxygenase polypeptide, a thrombomodulin polypeptide, a vascular endothelial growth factor, a chimeric p27-p16 polypeptide, a hepatocyte growth factor, a cytosine deaminase-5-flurocytosine polypeptide, a chimeric pRb2/p130 polypeptide, a p21 polypeptide, a p27 polypeptide, a p53 polypeptide, a dominant negative H-ras polypeptide, an eNOS polypeptide, an iNOS polypeptide, an active site inactivated factor VIIa polypeptide and a tissue factor pathway inhibitor polypeptide.

47. The method of Claim 45 wherein said targeting molecule is administered by retroviral gene delivery, adenoviral gene delivery or naked DNA injection.

48. The method of Claim 45 wherein said targeting molecule is administered using a gene gun, cationic liposomes, molecular conjugates or a catheter.

49. A method for modifying arteries in a mammal, comprising:

a) isolating arterial smooth muscle cells;

b) introducing a targeting molecule into said isolated arterial smooth muscle cells; and

c) introducing said arterial smooth muscle cells comprising said targeting molecule into said mammal.

50. The method of Claim 49 wherein said targeting molecule comprises:

a) a first nucleic acid sequence comprising a promoter region of EphrinB2; and

b) a second nucleic acid sequence encoding a polypeptide,

wherein said first nucleic acid sequence is operably linked to said second nucleic acid sequence.

51. The method of Claim 49, wherein said second nucleic acid sequence encodes a polypeptide selected from the group consisting of a herpes simplex virus thymidine kinase polypeptide, a non-phosphorylatable retinoblastoma polypeptide, a cyclin-dependent kinase inhibitor polypeptide, a mutant cyclin G1 polypeptide, a nitric oxide synthase polypeptide, a growth arrest homeobox, vascular cyclo-oxygenase polypeptide, a thrombomodulin polypeptide, a vascular endothelial growth factor, a chimeric p27-p16 polypeptide, a hepatocyte growth factor, a cytosine deaminase-5-flurocytosine polypeptide, a chimeric pRb2/p130 polypeptide, a p21 polypeptide, a p27 polypeptide, a p53 polypeptide, a dominant negative H-ras polypeptide, an eNOS polypeptide, an iNOS polypeptide, an active site inactivated factor VIIa polypeptide and a tissue factor pathway inhibitor polypeptide.

52. A method for modulating angiogenesis in a mammal, comprising administering to said mammal a composition comprising:

    a) an agent; and

    b) a substance which binds an arterial smooth muscle cell-specific surface molecule, wherein said arterial smooth muscle cell-specific surface molecule is EphrinB2, under conditions appropriate for binding of said substance to said arterial smooth muscle cell-specific surface molecule.

53. The method of Claim 52 wherein angiogenesis occurs in conditions selected from the group consisting of tumor growth and wound healing.

54. The method of Claim 52 wherein angiogenesis is inhibited.

55. The method of Claim 52 wherein angiogenesis is promoted.

56. The method of Claim 52 wherein said substance is an antibody or antigen-binding fragment thereof which binds EphrinB2.

57. The method of Claim 52 wherein said agent is an anti-angiogenic agent.

58. The method of Claim 52 wherein said agent is an angiogenic agent.

59. The method of Claim 52 wherein said agent is conjugated to said substance.

60. A method for modulating angiogenesis in a mammal, comprising administering to said mammal a targeting molecule, wherein said targeting molecule comprises a first nucleic acid sequence comprising a promoter region of EphrinB2 operably linked to a second nucleic acid sequence encoding a polypeptide.

61. The method of Claim 60 wherein angiogenesis occurs in conditions selected from the group consisting of tumor growth and wound healing.

62. The method of Claim 60 wherein angiogenesis is inhibited.

63. The method of Claim 60 wherein angiogenesis is promoted.

64. The method of Claim 60, wherein said second nucleic acid sequence encodes a polypeptide selected from the group consisting of a herpes simplex virus thymidine kinase polypeptide, a non-phosphorylatable retinoblastoma polypeptide, a cyclin-dependent kinase inhibitor polypeptide, a mutant cyclin G1 polypeptide, a nitric oxide synthase polypeptide, a growth arrest homeobox, vascular cyclo-oxygenase polypeptide, a thrombomodulin polypeptide, a vascular endothelial growth factor, a chimeric p27-p16 polypeptide, a hepatocyte growth factor, a cytosine deaminase-5-flurocytosine polypeptide, a chimeric pRb2/p130 polypeptide, a p21 polypeptide, a p27 polypeptide, a p53 polypeptide, a dominant negative H-ras polypeptide, an eNOS polypeptide, an iNOS polypeptide, an active site inactivated factor VIIa polypeptide and a tissue factor pathway inhibitor polypeptide.

65. A method for altering angiogenesis in a mammal, comprising administering to a mammal, in a therapeutically effective quantity, a composition which binds EphrinB2 expressed on arterial smooth muscle cells.

66. The method of Claim 65 wherein angiogenesis occurs in conditions selected from the group consisting of tumor growth and wound healing.

67. The method of Claim 65 wherein angiogenesis is inhibited.

68. The method of Claim 65 wherein angiogenesis is promoted.

69. The method of Claim 65 wherein said composition is an antibody or antigen-binding fragment that binds EphrinB2.

70. The method of Claim 69 wherein said antibody or antigen-binding fragment binds to the extracellular domain of EphrinB2.

71. An artificially prepared vessel comprising arterial smooth muscle cells, wherein said arterial smooth muscle cells comprise a recombinant nucleic acid which increases expression of ephrinB2 above endogenous levels.

72. A method for diagnosing the presence of a tumor comprising detecting the expression of EphrinB2 in blood vessels from a mammal and comparing said expression with a suitable control.